

APPLICANT: Oxford, et al.
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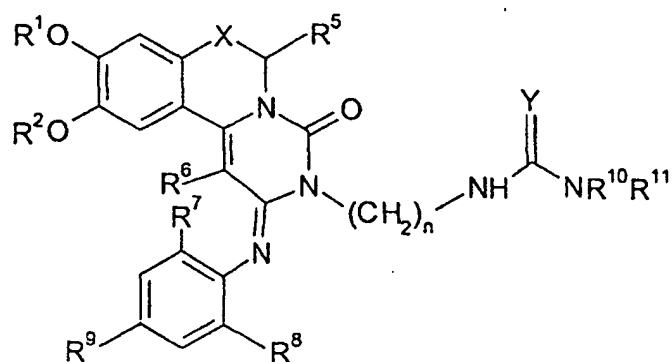
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This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

Claims 1-42 (cancelled).

Claim 43 (currently amended): A method for the treatment or prevention of a disease in a mammal where a phosphodiesterase isoenzyme inhibitor and/or a bronchodilator would be expected to be of benefit, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy,

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C₃₋₆ cycloalkyl; and

R⁹ represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy or C₃₋₆ cycloalkyl group;

X represents OCH₂ or a group CR³R⁴, wherein each of R³ and R⁴ independently represents a hydrogen atom or a C₁₋₃ alkyl group;

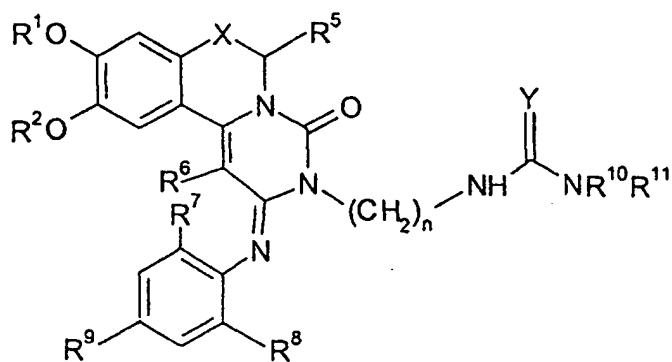
each of R¹⁰ and R¹¹ independently represents a hydrogen atom, a C₁₋₃ alkyl, C₃₋₆ cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO₂, NCN, NH or NNO₂;

n is an integer from 2 to 4;

or a salt thereof.

Claim 44 (currently amended): A method for the treatment or prevention of asthma in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

wherein

each of R¹ and R² independently represents a C₁₋₆ alkyl or C₂₋₇ acyl group;

R⁵ represents a hydrogen atom or a C₁₋₃ alkyl, C₂₋₃ alkenyl or C₂₋₃ alkynyl group;

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R⁶ represents a hydrogen atom or a C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, amino, C₁₋₆ alkylamino, di(C₁₋₆) alkylamino or C₂₋₇ acylamino group;

each of R⁷ and R⁸ independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl; and

R⁹ represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy or C₃₋₆ cycloalkyl group;

X represents OCH₂ or a group CR³R⁴, wherein each of R³ and R⁴ independently represents a hydrogen atom or a C₁₋₃ alkyl group;

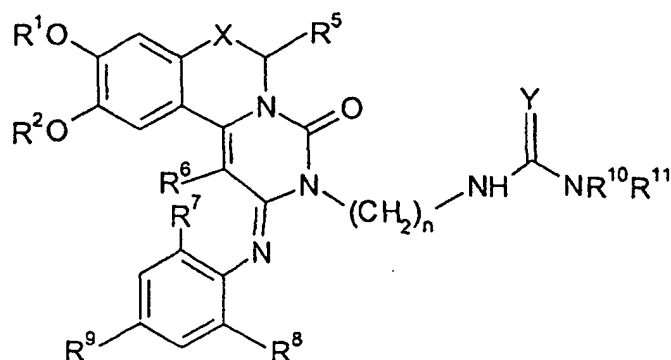
each of R¹⁰ and R¹¹ independently represents a hydrogen atom, a C₁₋₃ alkyl, C₃₋₆ cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO₂, NCN, NH or NNO₂;

n is an integer from 2 to 4;

or a salt thereof.

Claim 45 (currently amended): A method for the treatment or prevention of chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I:



I

wherein

each of R¹ and R² independently represents a C₁₋₆ alkyl or C₂₋₇ acyl group;

R⁵ represents a hydrogen atom or a C₁₋₃ alkyl, C₂₋₃ alkenyl or C₂₋₃ alkynyl group;

R⁶ represents a hydrogen atom or a C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, amino, C₁₋₆ alkylamino, di(C₁₋₆) alkylamino or C₂₋₇ acylamino group;

each of R⁷ and R⁸ independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl; and

R⁹ represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₂₋₆ alkynyl, C₂₋₇ acyl, C₁₋₆ alkylthio, C₁₋₆ alkoxy or C₃₋₆ cycloalkyl group;

X represents OCH₂ or a group CR³R⁴, wherein each of R³ and R⁴ independently represents a hydrogen atom or a C₁₋₃ alkyl group;

each of R¹⁰ and R¹¹ independently represents a hydrogen atom, a C₁₋₃ alkyl, C₃₋₆ cycloalkyl or phenyl group;

Y represents an oxygen atom or a group CHNO₂, NCN, NH or NNO₂;

n is an integer from 2 to 4;

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or a salt thereof.

Claim 46 (currently amended): A method as claimed in any of claims 43, 44 or 45, wherein the ~~compound is as defined in any of claims 1 to 15~~ independently or in any compatible combination:

each of R¹ and R² represents a C₁₋₆ alkyl;

R¹ and R² are the same as each other;

each of R³ and R⁴ represents a hydrogen atom;

R⁵ represents a hydrogen atom;

R⁶ represents a hydrogen atom;

each of R⁷ and R⁸ represents a C₁₋₆ alkyl;

R⁷ and R⁸ are the same as each other;

R⁹ represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group CHNO₂; and

n is 2.

Claim 47 (currently amended): A method as claimed in any of claims 43 to ~~46~~ 45, wherein the compound is administered by aerosol.

Claim 48 (currently amended): A method as claimed in any of claims 43 to ~~47~~ 45, wherein the animal is a human.

Claims 49-50 (cancelled).

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Claim 51 (new): A method as claimed in any of claims 43 to 45, wherein each of R¹ and R² represents a C₁₋₄ alkyl, group; and each of R⁷ and R⁸ represents a methyl, ethyl or isopropyl group.

Claim 52.(new): A method as claimed in any of claims 43 to 45, wherein the compound of general formula I is selected from the group consisting of:

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(*N*-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-isopropylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-methyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-isopropyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*, *N'*-dimethyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-phenylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-2-one;

9, 10-Dimethoxy-3-[2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

9,10-Dimethoxy-3-[*N*-(*N'*-nitro)-2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-[*N*-(*N'*-Cyclohexylcarbamoyl)-2-aminoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-(*N*-Carbamoyl-2-aminoethyl)-9,10-dimethoxy-2-(2-methylphenylimino)- 3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

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3-(*N*-Carbamoyl-2-aminoethyl)-2-(2,6-diisopropylphenylimino)-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one;

3-(*N*-Carbamoyl-4-aminobutyl)-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)- 3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one; and

3-[*N*-(*N'*-Cyano-*N''*-methyl)-2-guanidinoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-*a*]isoquinolin-4-one.